DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

DEC 21 2004

Warning Letter

Mrs. Lynda Nelson
President
Nelson Laboratories Incorporated
Post Office Box 17557
Salt Lake City, Utah 84117-0557

Dear Mrs. Nelson:

The purpose of this Warning Letter is to inform you of the objectionable conditions revealed during a Food and Drug Administration (FDA) inspection of your nonclinical testing facility. This letter also discusses your written responses dated August 18 and September 3, 2004, and requests that you implement prompt corrective actions in response to the violations cited. Ms. Ricki A. Chase-Off and Ms. Ginger M. Sykes, Investigators from FDA's Denver District Office, conducted the inspection on July 21, 22, 28, 29, and July 30, 2004. The purpose of the inspection was to determine if your laboratory's procedures complied with Title 21, Code of Federal Regulations (CFR) Part 58-Good Laboratory Practice (GLP) for Nonclinical Laboratory Studies. These regulations prescribe good laboratory practices for conducting nonclinical laboratory studies that support or are intended to support applications for research or marketing permits for FDA-regulated products.

Ms. Chase-Off and Ms. Sykes reviewed the following studies: [redacted] and [redacted]. At the close of the inspection, Ms. Chase-Off and Ms. Sykes presented a Form FDA 483 "Inspectional Observations" to [redacted], Laboratory Director, for review and discussed the listed deviations. The deviations noted on the Form FDA 483 and our subsequent review of the inspection report and your response are discussed below:

1. **Failure to adhere to the testing facility management requirements (21 CFR 58.31).**

   An example of this failure includes but is not limited to the testing facility management's failure to designate a study director prior to each study being initiated, as required by 21 CFR 58.31(a). Study Director [redacted] was responsible for subcontracted GLP studies at your facility; however, [redacted] was not designated by management on the Study Director Master List as an approved Study Director.

   Your response indicates that [redacted] coordinates subcontracted studies to other laboratories and does not oversee the overall conduct of the study. Your response

is incomplete, in that you have not provided documentation that shows the responsible study director for the studies overseen during [redacted] and [redacted]. For [redacted] subcontracted studies, [redacted] is listed as the study director but that is contrary to your stated response to the Form FDA 483. Therefore, with your response to this letter, please include documentation which reveals the study director for the [redacted] studies.

2. **Failure of Quality Assurance Unit to monitor each study to assure management that the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with applicable regulations (21 CFR 58.35(a), 58.35(b)(1), 58.35(b)(3), and 58.35(b)(5)).**

   Examples of this failure include but are not limited to the following:

   - The quality assurance (QA) unit failed to immediately inform the study director and management of problems likely to affect study integrity, as required by 21 CFR 58.35(b)(3). For example, studies [redacted] and [redacted] remained opened after being inactive for [redacted] or more months, and on several interim audit occasions, QA did not notify the study director or management of the inactivity.

     Your response appears to be adequate and indicates that you have cancelled the studies and included a mechanism in your revised Standard Operating Procedures (SOPs) for ensuring that appropriate attention is given to studies that are longer than [redacted] days.

   - The QA unit did not adequately monitor each study, as required by 21 CFR 58.35(a). For example:

     - The current test methods, which are described in SOP [redacted] have not been fully validated.
     - Two validations, [redacted] did not have the annual validation review completed, as required by SOP [redacted]
     - Particle monitoring for core cleanrooms was not performed every test session as required by SOP [redacted]
     - [redacted] sampling of viable airborne microorganisms for area [redacted] was not conducted as required by SOP [redacted]. The storage area was not sampled between [redacted] through [redacted].

     Your responses for the first, second, and third items above appear to be adequate. Upon further review of the particle count values used to certify

Cleanroom [redacted]; we find that the correct counts were used and your response to observation 3, item E on the Form FDA 483 appears to be adequate.

However, your response for the fourth item is inadequate, in that you have not provided the steps you have taken or plan to take to prevent the recurrence of not monitoring each study and auditing cleanroom data, which is required by 21 CFR 58.35(a) and part of the QA Unit responsibilities as required by SOP [redacted]

- Contrary to 21 CFR 58.35(b)(1), the QA unit failed to maintain copies of a master schedule sheet which contained all required elements, specifically the study status, for all nonclinical laboratory studies conducted by the testing facility. For example, the master schedule sheet for Study [redacted] does not reflect the current status of the study.

  Your response to this violation appears to be adequate.

- The QA unit failed to determine whether any deviations from approved protocols or SOPs had the proper authorization and documentation as required by your SOP [redacted] and 21 CFR 58.35(b)(5) . Study # [redacted] was not performed as a [redacted]' as required by SOP [redacted] Authorization describing the deviation from the SOP was not documented.

  Your response to this violation appears to be adequate.

3. **Failure to directly, promptly, and legibly record data generated (21 CFR 58.130(e)).**

   Your nonclinical site failed to directly, promptly, and legibly record data generated, as required by 21 CFR 58.130(e). For example:

   - Study # [redacted] did not have a record of the Study Director's findings related to the isolate failing to grow as required by the test protocol. There were lab notes for the incubation period of the isolates on [redacted] however, there were no further records indicating the progress of the study.

   - There was no record of the Study Director's findings for Study # [redacted] regarding test results not being reproducible and that the study would be discontinued.

   Your corrective action appears to be adequate; however, your preventative action is inadequate, in that the [redacted] review for the greater than [redacted] day inspections and the random selection by the [redacted] has not prevented the failure of recording data. Please provide in your response detailed steps of how you plan to ensure that data is reported for ongoing and future studies.

4. **Failure to establish adequate written standard operating procedures (SOPs) (21 CFR 58.81(a) and 58.81(b)).**

   Examples of this failure include but are not limited to the following:

   - SOP[redacted], does not include any steps that describe how to document and obtain approval of routine deviations from SOPs.

   - SOPs[redacted], do not address how to track samples or the movement of test articles in and out of the laboratory while a study is in progress.

   - SOP[redacted] does not require the QA unit to periodically provide written status reports for each study to the Study Director, as required by 21 CFR 58.35(b)(4).

   Your response to the above stated violations appears to be adequate.

   - There are no written procedures for handling of the test and control articles to ensure that receipt and distribution of each batch of investigational devices are documented, including the date and quantity of each batch distributed or returned.

     Examples of this failure include but are not limited to the following:

     - The number of specific samples/ampules sent to the sponsor for test exposure, or the number of samples/ampules received back from the sponsor were not documented for Study [redacted]

     - There was no documentation of the date that samples were returned to the sponsor for the study in Study #[redacted]

     - The receipt of [redacted] samples was incorrectly noted and the date returned to the sponsor was not recorded for Study #[redacted] as required by SOP[redacted]

   Your response is incomplete concerning the above listed violations. Training of employees who receive samples is a vital part of taking corrective and preventative action. Please provide a training plan and timeframes for training employees on SOP[redacted]. Also, provide a copy of the memo to the file, which relates to the failure to maintain the specific number of ampules sent to the sponsor.

5. **Failure to maintain an adequate summary of training and experience, and job description for each individual engaged in or supervising the conduct of a nonclinical laboratory study (21 CFR 58.29(b)).**

   Examples of this failure include but are not limited to the following:

   The testing facility failed to maintain a current summary of training, experience, and job description for each individual engaged in or supervising the conduct of a nonclinical laboratory study, as required by 21 CFR 58.29(b). For example, on April 28, 2004, the Chemistry Study Director I supervisor signed employee [redacted] training review record indicating that no action items were necessary. However, employee [redacted] did not have the annual GLP training required by SOP [redacted]

   Your response to this violation appears to be adequate.

6. **Failure to maintain written records of all inspection, maintenance, testing, calibrating and/or standardizing operations (21 CFR 58.63(c)).**

   The records documenting maintenance and calibration of the equipment were not adequate. For example:

   - The March 2003 Maintenance Schedule for equipment and calibration records for [redacted] and [redacted] do not indicate whether SOPs were followed for these activities.

   - The final report for [redacted] contained the incorrect temperature.

   Your response to these violations appears to be adequate.

The above-described violations are not intended to be an all-inclusive list of deficiencies that may exist at this nonclinical testing facility. It is your responsibility as a non-clinical laboratory to assure adherence to each requirement of the Act and all applicable federal regulations.

Within 15 working days after receiving this letter, please provide a corrective action plan and include written documentation of any changes and amendments since September 7, 2004, to address these violations and to respond to the Warning Letter. Failure to respond to this letter and take appropriate action could result in FDA taking regulatory action against you without further notice to you. Send your response to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Special Investigations Branch (HFZ-311), 2094 Gaither Road, Rockville, Maryland 20850. Attention: Doreen Kezer, Acting Chief, Special Investigations Branch.

We are also sending a copy of this letter to FDA's Denver District Office, 6th and Kipling Street, P.O. Box 25087, Denver, Colorado 80225-0087, and request that you also send a copy of your response to that office.

Please direct all questions concerning this matter to Ms. Kezer at (240) 276-0125.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health